

## Patterns and Management Challenges of Infertility in a Low-Resource Setting: A Prospective Cohort Study

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### Abstract

**Objectives:** To determine patterns and treatment outcomes of infertility among couples presenting with infertility in low-resource setting.

**Methods:** A prospective cohort study of infertile women managed at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria over a one-year period. Couples were followed up for a minimum of one year. Primary outcome measures were type/cause of infertility and conception rate. Univariate logistic regression was used to analyze data. Statistical significance was accepted when P-value is <0.05.

**Results:** During the study, 126 of 419 new patients managed were cases of infertility, giving an incidence of 30.1%. Mean duration of infertility was 4.1±3.9years. The ratio of primary to secondary infertility was 1:3, and maternal age, socio-economic status and infertility duration did not significantly influence the type of infertility ( $p>0.05$ ). Up to 55.6% (70/126) women had prior usage of herbal concoctions for infertility and was significantly influenced by infertility duration ( $p<0.001$ ). Conception rate was significantly more following ovulation factor infertility ( $p<0.001$ ). Up to 29.3% of couples achieved pregnancy within one-year follow-up.

**Conclusion:** The ratio of primary to secondary infertility was 1:3. Women with secondary infertility had significantly more conception rate. Overall, conception rate of 29.3% were achieved within one year of follow-up.

**Keywords:** Pregnancy; gynecological, primary; secondary; ovulatory disorder

### 1. INTRODUCTION

Infertility remains a threat to successful reproduction by couples desirous of pregnancy [1, 2]. Its problems are multidimensional and can impose profound physical, psychological and social strains on both partners in a couple [1-4]. The childless infertile women stand out as being vulnerable to the detrimental consequences of infertility [4]. When the treatment is unsuccessful, the couple may experience lower quality of life and high levels of stress, anxiety, and depressive symptoms [4-6].

It is noteworthy that in women having regular unprotected intercourse, conception occurs in 84% of them within 12 months and in 92% within 24 months [6]. Infertility is a worldwide problem affecting 8 – 15% of the couples in their reproductive age [7]. It is estimated that as many as 80 million couples are affected by infertility worldwide [8] and sub-Saharan Africa shares the largest burden of infertility worldwide [9].

However, the incidence varies from one region of the world to the other, being highest in the so-called infertility belt of Africa, of which Nigeria

is inclusive [9]. In some parts of this belt, infertility is said to constitute up to 65% of gynecological consultations [10]. Institution based incidence of infertility recently reported from some parts of Nigeria are: 4.0% [11], 11.2% [12] and 48.1% [13] respectively from Ilorin (North central), Abakaliki (south-east) and Oshogbo (South west).

The World Health Organization (WHO) had stated that where there is an infertility rate exceeding 15% of couples, it should be recognized as a public health problem [8]. While primary infertility is higher in other regions of the world, secondary infertility is more common in Africa [3]. In sub-Saharan Africa, pelvic infections largely constitute the cause of infertility in several places [9-13]. These stem from sexually transmitted diseases, post abortion and post-delivery complications. Comparative studies from Ile – Ife Nigeria showed a positive correlation between secondary infertility and induced abortion, post abortion sepsis, manual removal of placenta as well as previous prolonged unsupervised labor [14].

Both the males and females are said to contribute equally to infertility [10, 15]. Unfortunately in Nigeria, many men refuse or need much persuasion to present themselves for investigation either because they feel that they have no problem or as a result of their local/cultural beliefs [16]. Female disorders include cervical, uterine, tuboperitoneal, ovarian, endocrine and general metabolic disorders while male disorders include infection, ejaculation disorders, undescended testis and hormonal imbalances [10, 15].

Diagnosis of infertility depends on clinical presentation and results of investigations. So many advances in this field of gynecology have made investigative techniques for this condition vast and sophisticated. Unfortunately, clinicians in resource – poor settings face the challenge of harmonizing cost with efficient and effective management of infertility in this teeming population of patients [16]. All that may be available to the gynecologist may be a thorough history, physical examination and a few ancillary investigations.

The treatment of infertility consists of conventional methods as well as the assisted reproductive techniques (ART) [9]. ARTs are more recent methods, and have only begun to

gain grounds in Africa [9]. These techniques have been less well applied in many African countries due to inadequate facilities and the poor training of health personnel in infertility management.

Though knowledge about infertility is ever increasing daily, continued appraisal is necessary so that local data generated would be useful in counseling, investigating and management of these couples as well as help in proper and adequate health care plan for infertile couples. Currently, little is known about the status of infertility and its management in Nigerian hospitals. The objective of this study is therefore to determine the pattern of infertility, the common etiology, treatment outcomes and challenges among the patients presenting with infertility in a Nigerian tertiary hospital.

## **2. MATERIALS AND METHODS**

### **2.1. Study Area**

This study was conducted in Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi. NAUTH is a tertiary health institution that is located in the South-East Nigeria and serves as a referral centre for many gynecological cases. Majority of the cases of infertility managed were evaluated in the gynecology clinics, having been referred from the General Out-patient Department of the Hospital or from private hospitals in the environs due to various causes of infertility. Although NAUTH currently does not have facility for assisted reproduction such as in vitro fertilization (IVF) center, it has various facilities for management of gynecological cases including well equipped gyne-endoscopic surgery unit. Nnewi is a semi-urban town and the headquarters of Nnewi North Local Government Area of Anambra State, South-east Nigeria. The occupation of the people is mainly trading. Nnewi also has a handful of professionals as staff in the numerous financial and health care institutions. The people are predominantly Christians with a few traditionalists.

### **2.2. Study Population**

All adult patients who attended the gynecological clinic who were managed for infertility.

### **2.3. Inclusion Criteria**

All married women being managed for infertility.

#### **2.4. Exclusion Criteria**

Women who were not married and/or co-habiting with their male partners were excluded including women whose records could not be traced at follow-up period.

#### **2.5. Study Design**

This was a prospective cohort study of all infertility cases seen at the gynecological clinic of NAUTH between 1<sup>st</sup> January 2014 and 31<sup>st</sup> December 2014. All couples included in the study were followed-up from initial presentation till at least 12 months.

#### **2.6. Data Collection Methods**

Ethical clearance was obtained from NAUTH Ethics committee. Women for the study were interviewed and data collected immediately after the patients arrived at the gynecological clinic and identified as having complaint of infertility. Information was sought directly from the women and recorded in a structured proforma which included socio-demographic, past and present gynecological experience, gynecological history and examination findings and presumptive diagnosis. The names of the patients and their hospital numbers were obtained. Subsequently, on the follow-up basis, laboratory investigation results, treatment outcomes and follow-up patterns were determined. Some women who are willing were also contacted on phone when necessary. The treatment given was individualized and each patient was seen by at least a senior registrar. Each couple seen at the gynecological clinic was evaluated by at least three investigations viz: seminalysis for male factor assessment, transvaginal/abdominal ultrasound for folliculometry for ovulation assessment and hysterosalpingography and or laparoscopy and dye test for tubal patency assessment. Ovulation was accepted when the (pre-ovulatory) follicular size diameter is at least 18 mm. In those with abnormal findings at ovulation scanning (folliculometry), relevant hormonal assays are requested according to the gynecologist's judgement.

#### **2.7. Variables**

Socio demographic variables included: age, parity, highest educational level of the woman and occupation of the husband and type of infertility. The past gynecological variables included: previous miscarriage, termination of pregnancy, pelvic surgery, dilatation and

curetage, history of prior usage of herbal concoctions for fertility and duration of infertility. The social class was derived from the Olusanya, Okpere, Ezimokhai protocol of social classification [17].

The treatment outcome included: pregnancy, ongoing follow-up and or lost to follow-up. Abnormal semen parameters include: (sperm count <20 million/mL, motility <50%, morphology <30% [normal: World Health Organization criteria]) [18]. Infertility is the inability of a couple to achieve pregnancy over an average period of one year despite adequate, regular unprotected sexual intercourse. In primary infertility, the couples have never been able to conceive; while in secondary infertility there is difficulty in conceiving after having conceived (either carried the pregnancy to term or had a miscarriage). Unexplained infertility is diagnosed where routine investigations including semen analyses, tubal evaluation and tests of ovulation yielded normal results. A patient was said to be lost to follow up if not seen again at the outpatient clinic for six months from the last visit.

#### **2.8. Data and Statistical Analysis**

Data were entered after checking completeness, cleaning and coding into EXCEL spread sheet and analysed using computer EPI-Info 2013 version 7 (v 7; Epi Info, Centers for Disease Control and Prevention, Atlanta, GA). The results were analysed further using cross tabulation to explore statistical relationships between variables. Statistical analyses were performed using Student's *t*-test for continuous variables and the Fisher's exact tests for categorical data. A *P*-value of <0.05 was considered statistically significant. Data were presented as means, standard deviations (SD), numbers and frequencies (%). A probability value of <0.05 was considered significant.

### **3. RESULTS**

During the one year study period, 131 women were recruited. Five of the recruited women were excluded from the analysis because their case files could not be traced during the follow-up period, thereby yielding a final achieved sample of 126. Also, during the study period, a total of 419 new cases were seen in the gynecological clinic, although a total of 1463 cases (both old and new) were seen during the entire study period. Infertility accounted for

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31.3% (131/419) of all new gynecological cases seen in the gynecological clinic of the hospital.

The mean age of the women was  $35.1 \pm 7.1$  years (range=18-55 years) with 62.7% (79/126) of

them between 31 and 45 years of age. Majority, 53.2% (67/126) have secondary level of education. The socio-demographic characteristic of the respondents' is shown in table 1.

**Table1:** Socio-Demographic Characteristics of the Women

Variables	Frequency (N=126)	Percentage
<b>Age (years)</b>		
16-20	1	0.8
21-25	6	4.8
26-30	30	23.8
31-35	32	25.4
36-40	28	22.2
41-45	19	15.1
46-50	8	6.3
51-55	2	1.6
<b>Parity</b>		
0	69	54.8
1	30	23.8
2-4	23	28.2
$\geq 5$	4	3.2
<b>Educational level</b>		
Primary	4	3.2
Secondary	67	53.2
Tertiary	55	43.6
<b>Social Class</b>		
I	8	6.3
II	41	32.5
III	60	47.6
IV	13	10.3
V	4	3.2

A total of 26.2% (33/126) of the women had primary infertility at the initial fertility evaluation, and 73.8% (93/126) had secondary, giving a ratio of primary to secondary infertility as 1: 3. Majority of the women 61.1% (77/126) were from low social class. The age of the women, socio-economic status and duration of infertility did not significantly influence the type of infertility ( $P > 0.05$ ). The overall duration of infertility was mostly between 1 to 4 years in 65.9% of cases (83/126) with a mean duration of  $4.1 \pm 3.9$  years.

Majority, 54.8% (69/126) of women were nulliparous while 50.0% (63/126) of the women had had at least one episode of spontaneous miscarriage event. Of the 63 women that have had miscarriage, 52.4% (33/63) have had two or more episodes of spontaneous miscarriage. However, prior to presentation, 30.2% (38/126) of the women has had termination of pregnancy by dilatation and curettage (D&C) while 69.8% (88/126) had not. Table 2 shows the details of some past obstetrics and surgical characteristics of the women.

**Table2:** Some obstetrics and surgical characteristics of the women

Variable	Frequency	Percentage
<b>Number of miscarriages (N=63)</b>		
1	30	47.6
2	15	23.8
$\geq 3$	18	28.6
<b>Prior Dilatation and Curettage (D&amp;C) (n=126)</b>		
Yes	38	30.2
No	88	69.8
<b>Prior abdominopelvic surgeries</b>		
Yes	61	48.4
No	65	51.6

Of the 126 women, 55.6% (70/126) had used herbal concoctions prior to presentation while

44.4% (56/126) had not used. There is statistically significant relationship between the



duration of infertility and use of herbal concoctions ( $p < 0.05$ ). Women whose infertility had lasted at least 5 years had significantly higher chance of using herbal concoctions. The

**Table 3:** *The relationship between duration of infertility and type of infertility and usage of herbal concoctions*

Variable	Duration of Infertility (years)				
	1	2	3	4	$\geq 5$
<b>Type of infertility</b>					
Primary	3	10	7	4	9
Secondary	12	28	9	10	34
p-value	0.409	0.574	0.084	0.526	0.227
<b>Use of Herbal Concoctions</b>					
Yes	2	13	13	8	34
No	13	25	3	6	9
P-value	$< 0.001$	0.002	0.029	0.916	$< 0.001$

Of the 126 women, 44 (34.9%) absconded after the first initial visit and never returned for follow up thereafter. Of the 82 (65.1%) patients who continued, 23 (29.3%) were able to achieve pregnancy, 4 (4.9%) were referred to another hospital with facilities for assisted conception, 17 (20.7%) were still attending the gynecological clinic for follow up while 37 (45.1%) were lost to follow up, that is not seen 12 months from the last visit. Women diagnosed with an ovulatory disorder alone were significantly more likely to achieve a pregnancy compared to women with all other diagnoses as at least 12 months ( $P < 0.001$ ).

Seventy five (59.5%) of the 126 couples had the three basic investigations done (tubal patency test, seminal fluid analysis and ultrasound for folliculometry). The others had one, two or no investigations done for reasons ranging from monetary constraints, and husbands declining to do seminal fluid analysis.

Among the 75 couples that completed the three basic investigations, female factor was solely the cause of infertility in 43 (57.3%); male factor only in 12 (16.0%); both male and female factors in 13 (17.3%) and no identifiable causes (unexplained) in 7 (9.4%) couples.

Of the 43 couples with female factor only infertility, 19 (44.2%) had tubal factor as the cause, 8 (18.6%) were as a result of ovarian factor, 7 (16.3%) were as a result of uterine factor, 2 (4.7%) had cervical factor, 1 (2.3%) peritoneal while the remaining 6 (14.0%) were as a result of a combination of tubal, ovarian and uterine abnormalities.

Of the 75 women who had tubal patency done using hysterosalpingography ( $n=71$ ) and laparoscopy and dye test ( $n=4$ ), fifty seven (76.0%) had tubal occlusion (either unilateral in

relationship between duration of infertility and type of infertility and usage of herbal concoctions is shown in table 3.

29 cases or bilateral in 28 (49.1%) cases) of which six had at least one previous history of induced abortion. Eighteen had bilateral tubal patency, out of which 17 did not have prior history of induced abortion by dilatation and curettage. This was however statistically significant ( $p < 0.001$ ).

Of the 88 women who had ultrasound for folliculometry, 48 (59.3%) were normal, 33 (40.7%) had abnormal findings suggestive of anovulation.

Of the total of 81 men that had seminal fluid analysis, 47 (58.0%) were normal, 13 (16.0%) had oligozoospermia, 12 (14.8%) had asthenozoospermia, 5 (6.2%) had azoospermia while 4 (4.9%) had mixed pathology comprising oligo-astheno teratozoospermia.

#### 4. DISCUSSION

This study is very relevant because the World Health Organization (WHO) has repeatedly requested research on infertility in Africa [8]. The incidence rate of 31.3% of infertility found in this study is similar to 26.8% by Adegbola and Akindele<sup>5</sup> in Lagos but higher than 14.8% by Olatunji and Sule-Odu in southwestern Nigeria [19]. It is also higher than 5.5% reported by Ugwu et al [20] in Enugu, 8.0% by Safarinejad in Iran [21] and 15.4% by Rostad et al in Norway [3]. The status of our hospital as a referral center for most difficult infertility cases might be responsible for this high incidence.

The mean duration of infertility before presentation was  $4.1 \pm 3.9$  years. This is slightly lower than the mean duration of  $4.3 \pm 3.4$  years as reported by Adegbola and Akindele [5] in Lagos, Nigeria and  $7.5 \pm 6.0$  years by Audu et al in Gombe in Nigeria [22]. The observed difference noted in these studies might be due to

socio-cultural factors in different regions of the country as well as the fact that couples with infertility do not seek specialist care in those centers first. They would rather present first to general practitioners, wait passively or seek unorthodox care like traditional medical practitioners or healers before presenting to a specialist. These may also be the reason why majority of the women presented with prior intake of herbal concoctions. This is because, as seen in this study, women whose infertility had lasted at least 5 years had significantly higher chance of using herbal concoctions ( $p < 0.05$ ).

The mean age of the women at presentation was  $35.1 \pm 7.1$  years (range=18-55 years) with of 62.7% (79/126) of female partners between 31-45 years. This was similar to mean age of  $34.1 \pm 4.9$  years reported by Ugwu et al [20] in Enugu, Nigeria but quite higher than  $33.8 \pm 5.2$  years reported in Lagos [5] and  $28.3 \pm 6.0$  years in Gombe [22], all in Nigeria. Cultural differences in age at marriage could largely be responsible.

Generally, the prevalence of primary infertility is relatively low throughout sub-Saharan Africa [23]. Secondary infertility occurred in as high as 73.8% of couples in this study which is similar to other studies where secondary infertility accounted for 78.3% [19] in Ibadan, 80.0% [5] in Lagos, and 76.8% in Enugu [20], all in Nigeria. These findings are in quite contrast to studies from the western world where the incidence of primary infertility is higher. For example, the incidence of primary infertility was higher than secondary in Thailand (61.8%) [24], Sweden [25], and Iran [21]

In some countries, including Lithuanian [26], the percentage of men and women that encounter fertility problems is nearly the same. Female infertility constitutes 30-40% of cases, male infertility (10-30%), both partners (15-30%) and unexplained infertility (5-10%). This pattern is not in keeping with our present study where the female factor infertility alone predominates in approximately 60% of cases. The possible reasons for this peculiar finding are that the female factors are more commonly studied in Africa [23]. This is because it is commonly assumed that the woman is primarily responsible for infertility. Additionally, fewer men attend gynecological clinics for infertility management because they believe only women are responsible for infertility [23]. The male factor when it is predominant is associated with

a greater percentage of cases of primary rather than secondary infertility although this was not demonstrated in our findings [27].

In infertility, tubal disease represents the aftermath of pelvic infection or surgery resulting in tissue damage, scarring and adhesion formation. This can affect tubal function and result in either partial or total tubal occlusion. In some European countries such as Denmark, Finland and Belgium more than 4% of all children are born with the help of assisted reproduction [19]. However, the best treatment for women with tubal blockage is in vitro fertilization (IVF) and embryo transfer. Thus, tubal factor infertility remains the most common cause of female factor infertility in our cohort of couples studied with approximately 50% of women with tubal factors having bilateral tubal blockade. This will also explain why up to 5 couples in our data set were referred for assisted reproduction [1, 2]. Unfortunately, such patients could not complete their treatment in our hospital due to non-availability of IVF facility.

In this study, a number of factors might explain why the greater number of women had tubal factor infertility. This may be due to increasing number of women having prior history of abdomino-pelvic surgery and dilatation and curettage. This is worthy of note because prior to presentation, 30.2% of the women have had termination of pregnancy by dilatation and curettage (D&C) and there was statistically significant relationship between D&C and tubal blockage. Although the principal cause of tubal disease is pelvic inflammatory disease which may occur spontaneously, tubal blockade may also occur as a complication of miscarriage, puerperium, intrauterine instrumentation and pelvic surgery which were seen some of the women studied.

The number of spontaneous miscarriages observed in this study may be a reflection of uterine factor inherent in these women that presented with infertility. This is because 16.3% of couples with female factor infertility alone were as a result of uterine factor, while 52.4% of all infertile women have had at least two histories of spontaneous miscarriages. In a recent retrospective review of reproductive performance in patients with untreated uterine anomalies, it was suggested that these women experience high rates of miscarriage and preterm delivery in the presence of uterine factor [28].

Male factor infertility implies a lack of sufficient numbers of competent sperm, resulting in failure to fertilize the normal ovum. Previous studies of males attending an infertility clinic at the University of Nigeria Teaching Hospital (UNTH) Enugu, Eastern Nigeria showed that the etiology of male infertility in the population seem to be unrelated to sperm volume but related to sperm count, motility and morphology [29]. Interestingly, this experience was corroborated by our findings in this study where oligozoospermia (14.8%) was the most common abnormality. A similar result was observed in an infertility clinic in Lagos Southwestern Nigeria as reported in Ogunbanjo et al [30]. Additionally, a descriptive analysis of the seminal patterns of infertile males at the University College Hospital, Ibadan, in South-west Nigeria showed that asthenozoospermia was the most common seminal quality abnormality [31].

It is surprising that even in this study, approximately 8% of the women were between 46 and 55 years. This is because the upper limit of 46 – 55 years is the age menopause sets in which averagely in this environment, is 46 years. Although each gynecologist may view management options in women at perimenopause differently, generally, such women are best counseled for IVF or adoption.

Although the conception rate of 29.3% was seen in this study after at least one year of follow-up, up to 45.1% loss to follow-up was observed in this study. This value is not only high but shocking indeed and constitutes a big challenge in the management. Similar high rate of loss to follow up was observed by Adegbola et al [5] in Lagos, Nigeria. The reasons for this are not farfetched. The probable reasons include the fact that infertility investigation is quite expensive especially the laparoscopy and dye test and hormone assays. Again, poor medical insurance coverage makes a large numbers of these insurance providers unwilling to bear the cost of such investigations. Some inherent cultural beliefs might also be responsible for this trend.

The strength of this study is that it is one of the few studies on issues of infertility conducted in Nigeria including its prospective design which enabled verification of data directly from the women/couples. The weakness of the study is that the survey sample is limited in number since the majority of infertile couples would like to remain anonymous and preserve their

confidentiality, and even some decided to be lost to follow-up due to lack of consent to phone contacts. Another limitation of this study is that only couples that presented to the tertiary hospital participated in this study and so the general population may have been schewed. Furthermore, this study was subjugated by female respondents since it was the women that presented to the clinic in the preponderance of time while it would have been advantageous if the male partners presented to the clinic at the same rate as their female counterparts.

## **5. CONCLUSION**

Infertility constitutes approximately 30% of all new cases seen in gynecological clinic in Nigeria and one in every three infertile women has primary infertility. Women with secondary infertility were statistically more likely have prior history of intake of herbal concoctions and more conception rate following treatment than their primary infertility counterparts. Female factor was solely the cause of infertility in majority of cases with tubal factor predominating although 29.3% of women were able to achieve pregnancy.

**Human Rights Statements and Informed Consent:** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all patients for being included in the study.

## **Approval by Ethics Committee**

The teaching hospital ethics committee approval was gotten before the start of work. The study protocol was approved by the Institutional Review Board of Nnamdi Azikiwe University Teaching Hospital.

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